

Wine and Ocular Health

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Master Court of Sommeliers
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Understanding Wine

- Ocular health benefits
- General health benefits
- Risks of excessive drinking

Wine and Ocular Health

- The French Paradox
- Heavier foods, creams and meats in diet
- Longer life expectancy than in the US
- Develop cataracts later in life (?)

H

Wine and Ocular Health

- 1045 Subjects
- Compared through photofluormetry, the density changes in cataracts
- 22% for moderate wine consumption
- 32% for no wine consumption

H Sasaki, F Jonasson, Y Suwa et al. The Protective Effect of Wine Intake on Five Year's incidence of Cataract – Reykjavik Eye Study. ARVO Wed May 04, 2005 Abstract/Poster# 3840/B198

Wine and Ocular Health

- 3072 adults 45 to 74 years of age with macular changes indicative of AMD
- National Health Administration Eye Health survey & funduscopy
- The researchers observed a statistically significant negative association between AMD and alcohol consumption ($p < 0.01$)
- No benefit to beer or hard liquor – only wine in moderate consumption

Obisesan TO, Hirsch R, Kosoko O et al. Moderate wine consumption is associated with decreased odds of developing age-related macular degeneration in NHANES-1. Journal of the American Geriatric Society. 1998 Jan;36(1):1-7

Wine and Ocular Health: Resveratrol

- Can be consumed as a supplement or in red wine in particular
- Is a phytoestrogen
- Shown to fight inflammation, prevent oxidation of certain cells and prevent apoptosis

Wine and Ocular Health: Cataracts

- An experimental cataract model on lab rats
- It has been shown that a subcutaneous injection of selenite can induce senile cataract development.
- In the study rats were either injected with normal saline, Sodium selenite alone or sodium selenite with 40mg/kg of resveratrol.
- Cataract development was graded 11 days later using photography and the lenses were analyzed for lipid peroxidation, a marker present in cataract development

Doganay S, Boranzan M, Iraz M et al. The effect of resveratrol in experimental cataract model formed by sodium selenite. *Current Eye Research*. 2006 Feb;31(2):147-53

Wine and Ocular Health: Cataracts

- The results showed that all the control crystalline lenses (Saline injection) were clear as expected, the lenses in group two (selenite injection) had a 100% incidence of cataract and all were graded as grade 3 to 6 (6 being the highest)
- Finally in group 3 in which the rats also received resveratrol, 7 of the 16 animals showed 0% cataract development and of the remaining 9 they were all graded at 3 or less
- This was statistically significant ($p < 0.05$)

Doganay S, Boranzan M, Iraz M et al. The effect of resveratrol in experimental cataract model formed by sodium selenite. *Current Eye Research*. 2006 Feb;31(2):147-53

Wine and Ocular Health: AMD

- Antioxidant and antiproliferative effects of resveratrol were examined in a human RPE cell line
- The results showed that treatment with 50 and 100 micromol/L resveratrol significantly reduced proliferation of RPE cells by 10% and 25% respectively ($P < 0.05$)
- Resveratrol was shown to inhibit intracellular oxidation and protect the RPE cells from cell death

King RE, Kent KD, Bomser JA. Resveratrol reduces oxidation and proliferation of human retinal pigment epithelial cells via extracellular signal-regulated kinase inhibition. *Chemistry and Biology Interaction*. 2005 Jan 15;151(2):143-9

Wine and Ocular Health: AMD

- The observed reduction in cell proliferation was associated with inhibition of protein kinase
- Protein kinase was shown to be inhibited with resveratrol concentrations as low as 5 micromol/L
- These results suggest that resveratrol can reduce oxidative stress and hyperproliferation of the RPE cells of the retina.

King RE, Kent KD, Bomser JA. Resveratrol reduces oxidation and proliferation of human retinal pigment epithelial cells via extracellular signal-regulated kinase inhibition. *Chemistry and Biology Interaction*. 2005 Jan 15;151(2):143-9

Wine and Ocular Health: AMD

- In one paper, researchers have found that a combination of grape seed proanthocyanidin (tannins in red wine) and resveratrol prevents inducible secular endothelial growth factor (VEGF) expression, a key element supporting angiogenesis
- Anti-VEGF therapy is the basis for all the current wet AMD therapies such as Avastin

Sen CK, Khanna S, Gordillo G et al. Oxygen oxidants and antioxidants in wound healing: an emerging paradigm. *Annual NY Academy of Science*. 2002 May;957:239-49

Wine and Ocular Health: Cornea

Research has shown resveratrol's ability to suppress the enzyme MMP

MMP has been found to be an instrumental in causing recurrent corneal erosion and persistent epithelial defects

This study also went on to show that resveratrol is able to actually reduce corneal neovascularization in mice eyes

Oak MH, El Bedoui J, Chini-Kerth VB. Antiangiogenic properties of natural polyphenols from red wine and green tea. *Journal of Nutritional Biochemistry*. 2005 Jan;16(1):108

Wine Descriptor: Black Currant / Cassis



"Cassis" or black currant flavor of wine

Black currant is source of malvidin, an anthocyanin found in wine (anthocyanins = purple antioxidant pigment; type of polyphenol)

Seeds of black currant also deliver **GLA** – unique omega fatty acid found to relieve dry eye in 7 controlled clinical trials

Supplemental GLA for Dry Eye: 7 Controlled Clinical Trials

Aqueous-deficient (Barabino S et al. *Cornea* 22: 97–101, 2003.)

PRK (Macri A et al. *Graefes Arch Clin Exp Ophthalmol* 241:561-6, 2003.)

Sjögren's (Aragona P, et al. *Ophthalmol Vis Sci* 46:4474-9, 2005.)

Contact lens (Kokke KH et al. *Contact Lens Ant. Eye* 31:141-6, 2008.)

MGD (Pinna et al. *Cornea* 26:260-264, 2007.)

Mild-moderate DE (Brignole-Baudouin et al. *Acta Ophthalmologica* 89:e591-7, 2007.)

Post-menopausal women (**HydroEye**) (Sheppard JD, Pflugfelder SC, et al. *Cornea* 32 :1297-1304, 2013.)

Why not just fish oil for dry eye?

GLA: more compelling array of evidence (vs. Fish oil – with fewer DE studies, often small doses in non-representative populations, e.g. Northern India, Iran)

GLA has specificity for DE that fish oil omegas lack.

HydroEye combines GLA + modest level EPA from fish oil, other nutrients / cofactors. GLA + EPA has complimentary effect on inflammation

Sheppard JD, Pflugfelder SC, et al. Long-term supplementation with n-6 and n-3 PUFAs improves moderate-to-severe Keratoconjunctivitis Sicca: A randomized double-blind clinical trial. *Cornea* 32:1297-1304, 2013.

Clinical Validation: Supplement with GLA for Dry Eye Relief

Long-term Supplementation With n-6 and n-3 PUFAs Improves Moderate-to-Severe Keratoconjunctivitis Sicca: A Randomized Double-Blind Clinical Trial

Sheppard JD, Pflugfelder SC, et al. *Cornea* 32:1297-1304, 2013.

Background: Keratoconjunctivitis sicca (KCS) is a chronic, progressive, and potentially blinding disease of the eye. It is characterized by a deficiency of aqueous tears, which leads to ocular surface dryness, irritation, and inflammation. The disease is most commonly associated with Sjögren's syndrome, but can also occur in isolation. The pathogenesis of KCS is multifactorial, involving both autoimmune and non-autoimmune mechanisms. Treatment options are limited, and the goal of therapy is to alleviate symptoms and improve quality of life. Omega-3 polyunsaturated fatty acids (n-3 PUFAs) have been shown to have anti-inflammatory properties and may be beneficial in the treatment of KCS. The purpose of this study was to evaluate the efficacy of a long-term supplementation with n-6 and n-3 PUFAs in improving symptoms and quality of life in patients with moderate-to-severe KCS.

Methods: This study was a randomized, double-blind, placebo-controlled trial. The study population consisted of 100 patients with moderate-to-severe KCS, as defined by a Schirmer-I tear test result of ≤ 5 mm/5 min and a conjunctival injection score of ≥ 2 . The patients were randomized to receive either a daily supplement of 1.2 g of n-3 PUFAs (EPA and DHA) and 0.6 g of n-6 PUFAs (GLA) or a matching placebo. The primary endpoint was the change in the conjunctival injection score at 12 weeks. Secondary endpoints included the change in the Schirmer-I tear test result, the change in the ocular surface dryness index (OSDI), and the change in the quality of life score. The study was conducted in a tertiary care ophthalmology clinic.

Results: The study population was well characterized and representative of patients with moderate-to-severe KCS. The patients in the n-6 and n-3 PUFAs group showed a significant improvement in the conjunctival injection score compared to the placebo group at 12 weeks. There was also a significant improvement in the Schirmer-I tear test result, the OSDI score, and the quality of life score in the n-6 and n-3 PUFAs group. The improvement in the conjunctival injection score was maintained at 24 weeks. The study was well tolerated, and there were no significant adverse effects.

Conclusions: Long-term supplementation with n-6 and n-3 PUFAs significantly improves symptoms and quality of life in patients with moderate-to-severe KCS. The improvement in the conjunctival injection score, the Schirmer-I tear test result, the OSDI score, and the quality of life score suggests that n-6 and n-3 PUFAs have a beneficial effect on the ocular surface in KCS. The study was well tolerated, and there were no significant adverse effects.



SUMMARY OF FINDINGS:

GLA supplement users showed:

- Significant improvement in irritation symptoms & significantly better symptom scores vs. placebo
- Significantly better corneal smoothness vs. placebo
- Significantly lower levels of inflammatory markers vs. placebo.

Sheppard JD, Pflugfelder SC, et al. Long-term supplementation with n-6 and n-3 PUFAs improves moderate-to-severe Keratoconjunctivitis Sicca: A randomized double-blind clinical trial. *Cornea* 32:1297-1304, 2013.



Sheppard JD, Pflugfelder SC, et al. Long-term supplementation with n-6 and n-3 PUFAs improves moderate-to-severe Keratoconjunctivitis Sicca: A randomized double-blind clinical trial. *Cornea* 32:1297-1304, 2013.

Wine + Omegas



Cross-sectional study looked alcohol intake and omegas from diet and supplements with coronary heart disease

Moderate wine consumption (not other alcohols) found to boost blood omega-3 levels from food and supplements

This may help explain the heart benefits conferred from drinking red wine

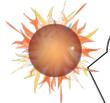
De Lorgeril, Michel, et al. "Interactions of wine drinking with omega-3 fatty acids in patients with coronary heart disease: a fish-like effect of moderate wine drinking." *American heart journal* 155.1 (2008): 175-181.

Antioxidants:

Primary health-promoting components in wine (especially reds)

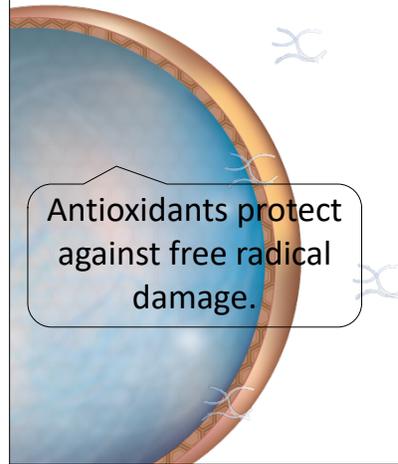
Note: following slides use vit C & E to show how antioxidants work – though C & E not found in wine specifically

How Antioxidants Work



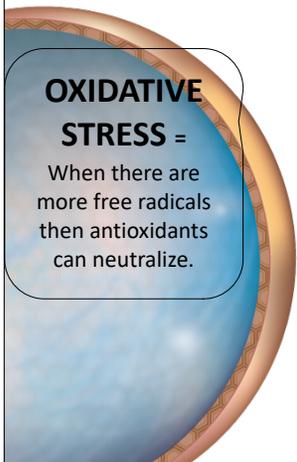
Free Radicals can damage cellular structures, contributing to health problems over time. Free Radicals (oxidative compounds) are generated during normal metabolism, as well as by outside sources (e.g. smoking, UV light)

How Antioxidants Work



Antioxidants protect against free radical damage.

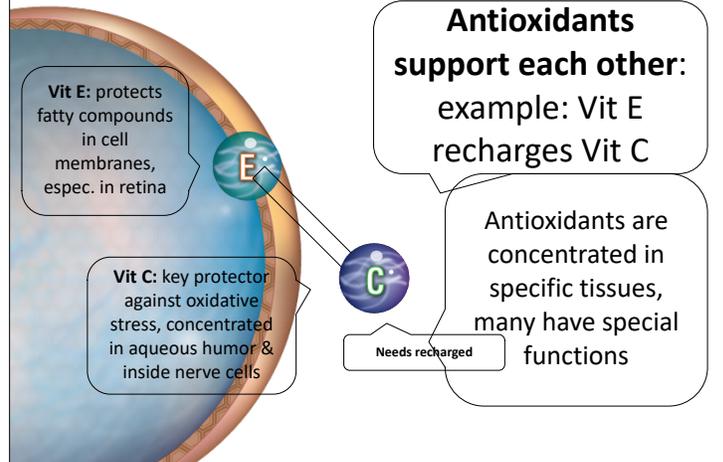
How Antioxidants Work



OXIDATIVE STRESS =

When there are more free radicals than antioxidants can neutralize.

How Antioxidants Work



Antioxidants support each other:
example: Vit E recharges Vit C

Vit E: protects fatty compounds in cell membranes, espec. in retina

Vit C: key protector against oxidative stress, concentrated in aqueous humor & inside nerve cells

Needs recharged

Antioxidants are concentrated in specific tissues, many have special functions

Quercetin + Myricetin

Human RPE cells, plus in animals:

Quercetin + myricetin combo superior vs either alone in reducing ocular inflammation

When combined with anthocyanins (purple-red antioxidant pigments found in berries), combo most effective in reducing endoplasmic reticulum stress – key risk factor for diabetic retinopathy

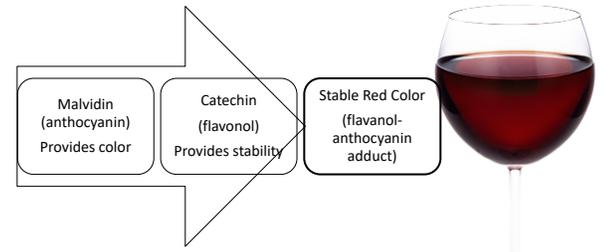
6. Ha JH, et al. J Nutr 144:799-806, 2014.

Wine Antioxidants: Seeing Red

Wine color comes from it's antioxidants!

Grape color components unstable.

During aging, complex interactions between antioxidants lead to stable red color. One example:



The taste of antioxidants



Tannins (and pseudo tannins) are polymers made up of antioxidant phenol and polyphenol compounds (including gallic acid, catechin, epicatechin).

Oak barrels are an important source of tannins, distinct from those provided by grape skins and seeds

Tannins impart a parched dryness at the front of your mouth, and can taste bitter near the middle of the tongue

Wine and Health

- One study went one to show that the tannins (polyphenolic antioxidants) in wine are effective in reducing myocardial ischemic reperfusion injury
- Plays a crucial role in cardioprotection
- Where do tannins in wine come from?

Das Dk, Sato M, Ray PS et al. Cardioprotection of red wine : role of polyphenolic antioxidants. Drugs Experimental and Clinical Resources. 1999;25(2-3): 115-20

Wine and Health: Fountain of Youth

- A study in mice found that resveratrol possessed pro-inflammatory properties and prevented the formation of blood clots
- Mice who consumed large quantities of the resveratrol compound, lived about 33% longer

Resveratrol improves health and survival of mice on a high-calorie diet. Nature. 2006 Nov 16;444(7117):337-42. Epub 2006 Nov 1.

Wine and Health: Excess Wine

- Been linked to an increase accidents and death
- 5-year Study of 14 western European countries, age and gender adjusted. Accidents were measured on a per consumption basis. Data confirmed that accident mortality rates were affected by per capita consumption[i].

▪ [i] Skog, OJ. Alcohol consumption and overall accident mortality in 14 European countries. Addiction. 2001 Feb;96. Suppl 1:S35-47

Wine and Health: Excess Wine

- Been linked to an increase in heart disease
- Research has shown that when looking specifically at Ischemic Heart Disease (IHD)
- Mortality rates were directly affected by consumption levels
- Ranged from protective effects with moderate alcohol consumption to harmful heart effects with heavy drinking

● Kerr WC, Ye Y. Population-level relationships between alcohol consumption measures and Ischemic Heart Disease mortality in U.S. time-series. Alcohol Clinical and Experimental Research. 2007 Nov; 31(11):1913-9

Wine and Health: Excess Wine

- Liver damage and excessive drinking
- More recent research has found that the main mechanism in liver cirrhosis is the activation of hepatic stellate cells, which acquire a myofibroblast-like phenotype.[1]
- Phenolic compounds contained in red wine have been shown to have antifibrotic properties, alcohol in excess can cause fibrosis to activated hepatic stellate cells resulting in cirrhosis

● Svegliati-Baroni G, Jezequel AM, Orlandi F. Wine: risk factors for liver disease and antibiotic compounds. Drugs Experimental and Clinical Research. 1999;25(2-3):143-5

Wine and Health: Excess Wine

- Epidemiological data have identified chronic, excessive alcohol consumption as a risk factor to cancers including those of the respiratory tract, upper gastrointestinal, liver, breast and colorectal.
- The pathophysiological mechanisms include acetaldehyde (AA), free-radical damage and loss of nutritional factors.

● Seitz HK, Maurer B, Stickel F. Alcohol consumption and cancer of the gastrointestinal tract. Digestive Diseases. 2005;23(3-4):297-303.

● Seitz HK, Meier P. The role of acetaldehyde in upper digestive tract cancer in alcoholics. Transl Resources. 2007 Jun;149(6):293-7

Wine and Health: Excess Wine

- Important for clinicians to assess the level of alcohol intake during a patient history
- The differences between daily intake of small to moderate alcohol versus large quantities may be the difference between preventing and causing disease
- 1-2 glasses per day, likely beneficial
- 1-2 bottles per day, likely NOT so good

Understanding and Health

- Resveratrol is also present in berries, grapes, nuts and grape juice
- Ounce for ounce, red wine packs two times more flavonoids
- The fermentation process allows resveratrol to be absorbed by the body more readily

Wine and Ocular Health

- Ocular health benefits
 - Retinal disease - AMD
 - Cataracts?
 - Corneal disease - RCE?
 - Other diseases that involve anti-VEGF?
- General health benefits -French Paradox
- Risks of excessive alcohol and optometry's role

Thank You

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